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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,226	01/20/2004	Philip C. Gevas	1102865-0031 CON	2197

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EXAMINER	
SEETHARAM, SARASWATHY	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/762,226	GEVAS ET AL.,	
	Examiner	Art Unit	
	Saraswathy Seetharam, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-5 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5 are pending. Claims 1-5 are examined on their merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph. Claim 2 recites the limitation "immunogen" which lacks antecedent basis in claim 1, because claim 1 recites " anti-G17 immunogenic composition" not immunogen. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by Watson et al.,(Int.J.Cancer ,1995 April, 61: pages-233-240).

Claims 1-4 drawn to a method of treatment of gastrin related tumors which comprises administering to a mammal an immunogenic composition which induces antibodies that neutralize gastrin-17 in vivo, wherein the tumors are colorectal adenocarcinomas expressing gastrin receptors.

Watson et al disclose a method of treating nude mice bearing xenografts of colorectal cancer cell line , AP5, that express gastrin/cholecystokinin receptors. Watson et al further disclose the anti-gastrin17 immunogenic composition which when administered to the mice (mammal) induced anti-G17 antibodies and neutralized the amidated and glycine extended gastrin-17.Watson et al teach that the anti-gastrin 17 immunogen when administered to mice bearing colorectal cancer xenografts inhibited the growth of the tumors. (see whole document).

Watson et al disclose that the anti-G17 immunogen is constructed of the N- terminal portion of human G17 conjugated to diphtheria toxoid and produces specific neutralizing anti-G17 antibodies (see page, 233, col.2. paragraph,2). Therefore, it is the Examiner's position that the anti-G17 immunogen , which Watson et al used in their study is the same as used by the applicant. One of ordinary skill would reasonably conclude that Watson's anti-G17 immunogen also possesses the same structural and functional properties as that of the immunogen and method of treatment for colorectal carcinomas claimed. Since the Patent and Trademark Office does not have the facilities for comparing the claimed immunogen, and it's efficacy in vivo , the burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the immunogen and method of treatment of the prior art. See In re Best, 562 F.2d 1252,195 U.S>P.Q 430 (CCPA 197) and Ex parte Gray, 10USPQ 2d 1922 1923 (PTO Bd. Pat. App.& Int.).

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Gevas et al.,(US Patent No. 5,468,494, filed 11/12/1993).

Claims 1-4 have been described supra. Claim 5 embodies the method of claim1 wherein the mammal is human.

Gevas et al., specifically disclose immunogenic composition of anti-gastrin 17 useful for controlling G17 levels in a patient by generating anti-gastrin antibodies and the use of such compositions for the treatment of gastrin-induced cancers. It further teaches that anti- G17 antibodies can be used to treat cancer in which G17 can be involved and that these antibodies can be induced in the patient by active immunization of the disclosed immunogenic composition. (col 1, lines 7-26).

The method of the prior art comprises the same method steps as claimed in the instant invention, that is, administering the anti-G17 immunogenic composition of the prior art to the same population, thus the claimed method will inherently lead to the treatment of gastrin related tumors whose growth is stimulated by amidated gastrin-17. Further, the active immunization produces antibodies which neutralize the physiological effects of amidated gastrin-17 appears to be the same as the prior art method. Therefore, it would be expected that that the antibodies would bind and neutralize amidated and glycine extended gastrin-17 because the immunogen against which the antibodies are raised comprises the aminoacid sequence of the molecule.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5 are rejected under 35 U.S.C. 103 as being unpatentable over Watson et al., (Int.J.Cancer, 1995 April, 61: pages-233-240) in view of Ladd et al.,(US patent No. 5,843,446, Filed 06/07/1995).

The claims are drawn to a method for the treatment of gastrin related tumors which comprises administering to a human subject an immunogenic composition which induces antibodies that neutralize the physiological effect of an immunogenic composition of anti –G17, wherein the tumors contain gastrin/ cholecystokinin B receptors, wherein the tumors are colorectal adenocarcinomas, wherein the mammal is a human.

Watson et al., teach a method for the treatment of colorectal cancers by administering an immunogenic composition of anti-gastrin 17(G17), to nude mice bearing xenografts of human colorectal cancer cell line AP5 which was shown to express both gastrin/cholecystokinin receptors and gastrin immunoreactivity. Watson et al teach the neutralizing ability of the immunogen (anti-G17 conjugated to diphtheria toxin, anti-G17:DT) through radio labeled immunogen and biodistribution studies (see page 236, In vivo analysis, fig. 3a). Further they teach the treatment of mice (mammal) bearing xenografts of AP5 with anti-G17:DT (see figs .5,6). Watson et al do not teach a method of treatment with the anti-G17 immunogen in humans having colorectal carcinomas. These deficiencies are made up in the teachings of Ladd et al.

Ladd et al., teach an immunogenic composition against human gastrin 17 coupled to an immunogenic carrier, (col.4, lines 49-55) and further teaches that specific antibodies neutralize the biological activity of disease promoting gastrin 17 which is involved in gastrointestinal disease processes including cancer and further teaches that anti-G17 antibodies can be used to treat cancers associated with an overproduction of gastrin (col.19 and 20) which G17 is involved and can either be administered to the human patient (i.e. passive immunization) or they can be induced in the patient by active immunization (col.21 lines 21-29).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have made improved immunogenic compositions of anti-gastrin17 to administer the immunogen in the treatment of colorectal carcinomas in humans which express the gastrin/cholecystokinin receptors in view of Ladd et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have administered the anti-G17 immunogen in effective amounts to humans, after evaluating the doses required to neutralize the circulating G17 in mice in view of Watson et al., because Watson et al teach the neutralizing effect of anti-G17:DT through biodistribution studies to determine the dosing schedule. In addition, one of ordinary skill in the

art would have been motivated and had a reasonable expectation of success to use the immunogenic composition in human patients to treat colon adenocarcinomas or provide protective immunity in view of Ladd et al., because Ladd et al teach methods of using the immunogenic compositions to treat human patients.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to use the anti-G17 immunogen in the treatment of patients with colorectal cancer to achieve in situ production of high affinity anti-G17 antibodies with the potential capacity to neutralize elevated gastrin levels.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Saraswathy Seetharam, PhD whose telephone number is 571-272-2113. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

Saraswathy Seetharam, PhD
Examiner
Art Unit 1642